THAT WHICH IS CLAIMED IS:

1. A method for determining the *in vivo* clinical efficacy of a treatment in a subject, comprising:

positioning at least one sensor in tissue in a region of interest in the body;

administering a fluorescent analyte to a subject, the fluorescent analyte including at least one of a fluorescently pre-labeled analyte, a naturally fluorescent analyte and an analyte that exhibits fluorescence when internally administered to the subject;

emitting at least one excitation light signal from the at least one sensor to tissue proximate the at least one sensor;

detecting *in vivo* from the at least one sensor a signal corresponding to the fluorescence in the region of interest in the subject responsive to the administering step;

relaying the signal to a location external of the subject's body; and

monitoring the signal over time to determine the localized fluorescence response of the subject to the administered fluorescently pre-labeled analyte, naturally fluorescent analyte and/or analyte that exhibits fluorescence when in the subject.

2. A method according to Claim 1, wherein the administrating step comprises administering the fluorescently pre-labeled analyte, wherein the excitation light is able to penetrate tissue that is up to about 20 mm away, and wherein the label is an excitation wavelength of from about 630 to about 660 nm that generates fluorescence response wavelengths of from about 665 to about 695nm.

3. A method according to Claim 1, wherein administering comprises administering the fluorescently pre-labeled analyte, wherein the excitation light is able to penetrate tissue that is up to about 20 mm away, and wherein the label is an excitation wavelength of from about 400 to about 660 nm that generates fluorescence response wavelengths of from about 400 to about 695nm.

4. A method according to Claim 1, wherein the at least one sensor is adapted to be implanted in the body at subsurface depths up to about 25 cm.

5. A method according to Claim 1, wherein the excitation light signal is generated by a pulsed laser diode.

6. A method according to Claim 5, wherein the pulsed laser diode is operated with a frequency that is between about 10 Hz to about 1 KHz and with a duty cycle of between about 1 to about 10 percent.

7. A method according to Claim 6, wherein the excitation signal has an associated operating level of from about 1 to about 20 mW.

8. A method according to Claim 1, wherein the at least one excitation signal comprises a plurality of signals having a predetermined variation in output intensity, and wherein the detected fluorescence is used to generate optical profiling data.

9. A method according to Claim 1, wherein the at least one sensor is configured as a cylindrical encapsulated body having a cylindrical optical filter that selectively allows light associated with the fluorescent wavelengths of interest to travel into the interior of the sensor body.

10. A method according to Claim 1, wherein administering comprises administering a fluorescently pre-labeled analyte, wherein the analyte is a therapeutic pharmaceutical drug configured to treat a selected physiologic or biologic condition, impairment, or disease, and wherein the fluorescence label is substantially transparent to the physiologic or biologic reaction of the drug in the body, and wherein said monitoring is carried out to predict and/or assess the *in vivo* clinical efficacy and/or localized dose of a selected treatment.

11. A method according to Claim 1, wherein the administrating step comprises administering the fluorescently pre-labeled analyte, wherein the analyte comprises an antibody configured to treat a selected physiologic or biologic condition, impairment, or disease, and wherein the fluorescence label is substantially transparent to the physiologic or biologic reaction of the antibody in the body, and wherein said monitoring is carried out to: (a) predict or assess the *in vivo* clinical efficacy of a

selected treatment; (b) measure the localized dose; and/or (c) adjust the therapeutic dose amount administered to the subject.

12. A method according to Claim 1, wherein the administrating step comprises administering the fluorescently pre-labeled analyte, wherein the pre-labeled analyte is a fluor-labeled pharmaceutical grade version of a gene therapy analyte configured for administration to a human subject, the labeled version of being substantially transparent to the *in vivo* behavior of the non-labeled version.

13. A method according to Claim 12, wherein the monitoring is carried out to determine the expression of a protein resulting from the administered gene therapy.

14. A method according to Claim 1, further comprising the step of processing the relayed signal to electronically generate a time-dependent measurement profile of fluorescence in the localized tissue.

15. A method according to Claim 1, wherein said monitoring step determines that at least one of the uptake and retention of the fluorescent analyte in the localized region is above a predetermined threshold level and/or the rate of the increase and decay in the signal strength over time.

16. A method according to Claim 1, further comprising determining a phenotypic response to the fluorescent analyte based on said monitoring step.

17. A method according to Claim 1, wherein said monitoring step determines the amount of time the detected signal remains above a threshold level, the time the signal takes to reach a peak level, the time the signal takes to decay to below a threshold value, and the rate of decay from the peak to the threshold value.

18. A method according to Claim 1, wherein said monitoring step monitors, over a period of at least about 1 hour from the time said administering step is initiated, is used to generate a time-response profile with at least one predictor variable derived therefrom associated with the uptake and/or retention of fluorescence in localized tissue, the predictor variable including at least one of:

(a) the time at which the detected peak fluorescence count occurs;

(b) the rate of increase of detected fluorescence;

(d) the rate of decrease of detected fluoresence;

(e) the time at which the detected fluorescence falls a predetermined amount below a threshold or the peak detected value;

(f) the duration that the detected signal increases in strength; and

(g) the time during the monitored period when the detected signal begins to decay.

19. A method according to Claim 1, wherein the fluorescent analyte is administered to the subject as a first test dose amount, said monitoring step predicts whether the response of the subject to the first dose indicates the likelihood of a favorable response to a selected treatment, and wherein said method further comprises the step of administering a second therapeutic dose of the fluorescent analyte to the subject if a favorable response is indicated, and wherein the second therapeutic dose amount is greater than the first test dose amount.

20. A method according to Claim 1, wherein administering comprises administering the fluorescently pre-labeled analyte and wherein said monitoring step assesses the behavior of the labeled analyte *in vivo* in the localized tissue and generates a predictive treatment outcome of a corresponding non-labeled analyte based on the monitored behavior of the labeled analyte.

21. A method according to Claim 1, wherein the sensor is disposed proximate or in a cancerous tumor, and wherein said monitoring step comprises determining cancer cell sensitivity or receptiveness to the fluorescent analyte.

22. A method according to Claim 1, wherein at least one of the at least one sensors is positioned in the body so as to be proximate a tumor, and wherein said administering step is first carried out at a time which is proximate to a first planned therapeutic treatment, and wherein said detecting step further comprises determining if the tumor is likely to be responsive to the planned treatment based on said detecting and monitoring steps, said method further comprising the steps of:

administering a therapeutic treatment to the subject after a first fluorescent analyte administering step; and

repeating said step of administering the fluorescent analyte after said step of administering a therapeutic treatment to monitor changes in cell kinetics following a therapeutic treatment.

23. A method according to Claim 1, wherein the step of positioning is carried out so that the sensor is chronically implanted in the subject.

24. A method according to Claim 1, wherein the at least one sensor is a plurality of sensors, each positioned in different locations in the body of the subject, and wherein each of the plurality of sensors can be serially polled.

25. A method according to Claim 1, wherein the step of positioning is carried out so that at least one sensor is positioned proximate to cancerous tissue and another sensor is positioned proximate to normal tissue, and wherein said detecting step detects the biokinetics of both normal and cancerous tissue.

26. A method according to Claim 1, wherein at least one of said sensors is implanted in localized tissue in the target region of interest and configured to operate wirelessly such that said relaying step is carried out telemetrically.

27. A method according to Claim 1, wherein administering comprises administering a fluorescently pre-labeled analyte, wherein the labeled analyte is a labeled version of a pharmaceutical product undergoing clinical evaluation, and wherein the clinical efficacy evaluated in said monitoring step comprises determining whether the pharmaceutical product reaches the region of interest and/or the pharmacodynamics and/or pharmacokinetics thereof.

28. A method according to Claim 1, wherein said detecting step is at least periodically performed over a period of time extending for at least between about 24-48 hours.

29. A method according to Claim 1, wherein said detecting step is at least periodically performed over a period of time extending from about several seconds to about several minutes.

30. A method according to Claim 1, wherein said monitoring step serially determines the fluorescent intensity of the fluorescent analyte in the localized tissue at a plurality of points in time and then determines at least one of the pharmacokinetic, the pharmacodynamic, the biokinetic response to the fluorescent analyte and/or the bioactivity in tissue in the region of interest.

31. A method of evaluating a subject, comprising:

administering a fluorescent analyte to a subject, the fluorescent analyte including at least one of a fluor-labeled analyte, a naturally fluorescent analyte and an analyte that exhibits fluorescence when internally administered to the subject;

repetitively emitting excitation light from an implanted sensor over a desired monitoring period;

detecting fluorescence intensity in response to the excitation light using the implanted sensor that outputs the excitation light;

using data associated with the detected fluorescence intensity to perform at least one of: (a) calculate the concentration or dose of the analyte received proximate to the implanted sensor; (b) evaluate the pharmacodynamic or pharmacokinetic activity of the fluorescent analyte; (c) confirm Ab attachment to a tumor site; (d) monitor a non-target site to confirm it is not unduly affected by a therapy; (e) monitor for changes in cellular properties; (f) use the calculated dose or concentration data to adjust or customize a therapeutic amount of an fluorescent analyte administered to the subject; (g) confirm micelle concentration at a target site and then stimulate toxin release based on the confirmation; and (h) monitor for the expression of a protein produced from a gene therapy modification.

32. A method according to Claim 31, further comprising varying the intensity of the excitation signals emitted to the localized tissue in a predetermined manner to generate optical profiling data of the response of the tissue proximate the sensor.

33. A method according to Claim 31, wherein the sensor is implanted in or proximate to a tumor.

34. A method according to Claim 31, wherein the sensor is adapted to be implanted at depths in the body up to about 5-25 cm below the skin of a patient.

35. A method according to Claim 31, wherein the sensor is adapted to be implanted at depths in the body between about 5-20 cm below the skin of a patient, the method further comprising pulsing a laser diode disposed in the implanted sensor to generate the excitation light.

36. A method according to Claim 31, wherein the sensor is adapted to be implanted at depths in the body from about 1 to about 25 cm below the skin of a patient, the method further comprising pulsing a laser diode disposed in the implanted sensor to generate the excitation light.

37. A method according to Claim 35, wherein the laser diode is operated with between about a 1-10% duty cycle to generate the excitation light.

38. A method according to Claim 37, wherein the repeated emissions of the excitation light and associated detecting steps are carried out at spaced apart intervals over at least 1 hour.

39. A method according to Claim 38, wherein the emitting and detecting steps are repeated at desired intervals over between about at least one 24-48 hour monitoring period.

40. A method according to Claim 31, wherein the emitting and detecting steps are repeated at desired intervals over from about a several seconds and about a several minute monitoring period.

41. A method according to Claim 31, wherein the detected data is used to carry out a plurality of operations (a)-(h).

42. A method according to Claim 31, wherein the detected data is used to carry out at least three of operations (a)-(h).

43. A detection system for detecting fluorescence in a subject associated with an internally administered fluorescent analyte, the fluorescent analyte including at least one of a fluor-labeled analyte, a naturally fluorescent analyte and an analyte that exhibits fluorescence when internally administered to the subject, the detection system comprising:

at least one fluorescence sensor configured for *in vivo* operation, the at least one sensor being configured to emit an excitation light signal and to detect fluoresence from a fluorescent analyte in localized tissue in the body in response to the emitted excitation light signal, at least intermittently, over a period of time extending for at least about 24 hours after administration of a fluorescent analyte; and

a processor operably associated with the at least one sensor configured to direct the output of the excitation signal and to receive fluorescence intensity signal data associated with the detected fluoresence from the at least one sensor, wherein said processor includes computer program code for monitoring intensity over time associated with one or more of the uptake and retention of the fluorescent analyte in the targeted localized tissue at a plurality of points in time over at least one monitoring period.

44. A system according to Claim 43, wherein the sensor is configured as an implantable telemetric sensor having an elongated substantially cylindrical body.

45. A system according to Claim 44, wherein the sensor has a body with a diameter of about 3 mm or less.

46. A system according to Claim 43, wherein the at least one sensor is configured to wirelessly transmit signals associated with the *in vivo* detected fluorescence at predetermined intervals extending over a monitoring period having a duration at least about 1 week.

47. A system according to Claim 46, wherein the at least one sensor is configured to wirelessly transmit signals associated with the *in vivo* detected

fluorescence at predetermined intervals, including a plurality of transmissions over a plurality of days during a monitoring period having a duration of at least about 1 month.

48. A system according to Claim 43, wherein the at least one sensor is a plurality of sensors, including first and second sensors that are adapted to detect fluorescence emitted from first and second spatially separate locations in the subject.

49. A system according to Claim 43, wherein the at least one sensor is a plurality of sensors configured to be individually operable, and wherein the processor is configured to poll each one separately.

50. A system according to Claim 48, wherein the first location is associated with normal or non-diseased tissue and the second location is associated with diseased, abnormal, or cancerous tissue.

51. A system method according to Claim 43, wherein the sensor is configured to generate excitation light that is able to penetrate tissue that is up to about 20 mm away.

52. A system according to Claim 43, wherein the sensor is configured to generate excitation light signals having a wavelength of from about 400 to about 660 nm.

53. A system according to Claim 52, wherein the sensor is configured to detect fluorescence response wavelengths of from about 400 to about 695nm.

54. A system according to Claim 43, wherein the at least one sensor is adapted to be implanted in the body at subsurface depths up to about 25 cm.

55. A system according to Claim 43, wherein the sensor comprises laser diode that is configured to generate the excitation light.

56. A system according to Claim 55, wherein the laser diode is operated in a pulsed manner to generate the excitation light.

57. A system according to Claim 56, wherein the pulsed laser diode is operated between at a frequency of from about 10Hz to about 1 KHz with a duty cycle of between about 1-10%.

58. A system according to Claim 56, wherein the laser diode is configured to generate an excitation signal with a power level of from about 1 to about 20mW.

59. A system according to Claim 43, wherein the system is configured to generate a plurality of signals having a predetermined stepwise variation in power, and wherein the detected fluorescence generated in response thereto is used to generate optical profiling data.

60. A system according to Claim 44, wherein the sensor further comprises a detector, and wherein the sensor body comprises a cylindrical optical filter formed on the wall thereof that selectively allows light associated with the fluorescent wavelengths of interest to travel into the interior of the sensor body to the detector.

61. A system according to Claim 60, wherein the sensor further comprises a compound filter aligned with the laser diode to allow the excitation light to exit the sensor body through the cylindrical filter.

62. A system according to Claim 60, wherein the sensor further comprises an optical window aligned with the laser diode to allow the excitation light to exit the sensor body through the cylindrical filter.

63. A system according to Claim 60, wherein the detector is substantially centrally located in the sectional width of the sensor body.

64. A system according to Claim 63, wherein the sensor is configured to allow fluorescence to enter and engage with the detector having a width that is between about 1.15 R to about 0.54 R, where "R" is the radius of the cross-section of

the sensor body, and wherein the cylindrical filter extends substantially continuously over the perimeter of the sensor body at a length that is less than the length of the sensor body.

65. A system according to Claim 43, wherein the excitation source comprises a laser diode and the detector comprises a photodiode, wherein the sensor body is a glass sensor capsule, and wherein the sensor further comprises epoxy that is index-matched to couple the laser diode and photodiode to the glass capsule enclosing the detector and diode to inhibit internal reflections.

66. A system according to Claim 65, wherein the sensor further comprises a second detector, wherein the first detector is operably associated with a filter that selectively allows fluorescent light signals to pass therethrough, and wherein the second detector is configured to detect excitation light signals, and wherein data from the second detector is used to normalize the data from the first detector.

67. A system according to Claim 66, wherein the sensor further comprises a second detector, and wherein the first and second detectors are held in side-by-side alignment in the sensor body.

68. A system according to Claim 67, wherein the sensor further comprises a second detector, and wherein the first and second detectors are held in back-to-back alignment.

69. A system according to Claim 43, wherein the excitation source comprises first and second diode lasers operating at different excitation wavelengths and/or power.

70. An implantable fluorescence sensor, comprising:

an elongated substantially cylindrical sensor body;

a cylindrical optical filter formed over the outer surface of the elongated sensor body;

at least one excitation light source held in the sensor body configured to generate excitation light from the sensor at a predetermined wavelength of interest having an power less than about 20mW; and

at least one detector held in the sensor body configured to detect fluorescence at predetermined wavelengths of interest,

wherein the sensor is configured to be intermittently operated at plurality of sampling intervals over a monitoring period of interest.

71. A sensor according to Claim 70, wherein the implantable sensor excitation source comprises a laser diode operated at a power between about 1-20mW.

72. A sensor according to Claim 70, wherein the sensor body comprises an optical window formed on the wall thereof to allow the excitation light to exit the sensor through the cylindrical filter.

73. A sensor according to Claim 70, further comprising a compound filter aligned with the excitation light source and formed about a portion of the cylindrical filter to allow the excitation light to exit the sensor through the cylindrical filter.

74. A sensor according to Claim 70, wherein the light source is positioned in the sensor body proximate the cylindrical wall at a distance and position that directs the excitation light out through the cylindrical filter at an angle greater than the critical angle to thereby allow the excitation light to exit the sensor through the cylindrical filter.

75. A sensor according to Claim 70, wherein the sensor is inductively powered.

76. A sensor according to Claim 70, wherein the sensor is telemetrically operated.

77. A sensor according to Claim 70, wherein the sensor is configured to output a plurality of excitation light signals and detect fluorescence generated locally

in response thereto over desired intervals over at least 24 hours for each monitoring period.

78. A sensor according to Claim 70, further comprising an anti-reflectance layer in the sensor body intermediate the wall of the sensor body and the underside of the detector.

79. A sensor according to Claim 70, wherein the laser diode is operated in a pulsed manner to generate the excitation light.

80. A sensor according to Claim 79, wherein the pulsed laser diode is operated between at a frequency of between about 10-1KHz with a duty cycle of between about 1-10%.

81. A sensor according to Claim 70, wherein the sensor is configured to generate a plurality of excitation signals having a predetermined stepwise variation in intensity, and wherein the detected fluorescence generated in response thereto is used to generate optical profiling data.

82. A sensor according to Claim 70, wherein the detector is substantially centrally located in the sectional width of the sensor body.

83. A sensor according to Claim 70, wherein the sensor is configured to allow fluorescence to enter and engage with the detector, with the detector having a width that is between about 1.15 R to about 0.54 R, where "R" is the radius of the cross-section of the sensor body.

84. A sensor according to Claim 70, wherein the cylindrical filter extends substantially continuously over the perimeter of the sensor body at a length that is less than the length of the sensor body

85. A sensor according to Claim 70, wherein the sensor further comprises a second detector.

86. A sensor according to Claim 85, wherein the first and second detectors are held in side-by-side alignment in the sensor body.

87. A sensor according to Claim 85, wherein the first and second detectors are held in back-to-back alignment.

88. A sensor according to Claim 70, wherein the excitation source comprises first and second diode lasers operating at different excitation wavelengths and/or power.

89. A computer program product for evaluating a subject's *in vivo* response to a fluorescent analyte, the fluorescent analyte including at least one of a fluorescently pre-labeled analyte, a naturally fluorescent analyte and an analyte that exhibits fluorescence when internally administered to the subject, the computer program product comprising a computer readable storage medium having computer readable program code embodied in said medium, said computer-readable program code comprising:

computer readable program code for directing the emission of at least one excitation light signal using a sensor into a subject about a local targeted site in the body of a subject at depths up to about 25 cm *in vivo* a plurality of times during a monitoring period having a duration of at least 1hour;

computer readable program code for serially receiving a plurality of fluorescence intensity count data detected *in vivo* in tissue proximate the target site from the sensor over time, the detected intensity data corresponding to fluorescence generated from tissue having a fluorescent analyte that is administered to a subject, responsive to exposure to the excitation light; and

computer readable program code for generating a time-dependent measurement profile for evaluating selected parameters associated with at least one of the signal intensity, concentration, uptake and retention of the fluorescent analyte in the localized tissue of the subject.

90. A computer program product according to Claim 89, further comprising computer readable program code for determining the likelihood that a

planned therapy will be clinically efficacious prior to delivery of the planned therapy based on the time-dependent profile.

91. A computer program product according to Claim 89, wherein said computer program product includes computer program code for initiating the emissions and receiving the detections a plurality of times over a monitoring period of at least about 24 hours.

92. A computer program product according to Claim 89, wherein said computer program product includes computer program code for initiating the emissions and receiving the detections a plurality of times over a monitoring period of at least about 48 hours.

93. A computer program product according to Claim 89, wherein said computer program product further comprises computer readable program code for calculating the concentration or dose of the fluorescent analyte delivered to the local targeted site.

94. A computer program product according to Claim 89, further comprising computer program code for calculating the concentration or dose of the fluorescent analyte received proximate to the implanted sensor site based on the plurality of received fluorescence intensity count data over time.

95. A computer program product according to Claim 89, further comprising computer program code for evaluating the pharmacodynamic or pharmacokinetic activity of the fluorescent analyte evaluating the pharmacodynamic or pharmacokinetic activity of the fluorescent analyte.

96. A computer program product according to Claim 89, further comprising computer program code for confirming antibody attachment to a tumor site.

97. A computer program product according to Claim 89, further comprising computer program code for monitoring a non-target site to confirm it is not unduly affected by an administered therapy.

98. A computer program product according to Claim 89, further comprising computer program code for monitoring for changes in cellular properties.

99. A computer program product according to Claim 89, further comprising computer program code for calculating dose or concentration and adjusting or customizing the therapeutic amount of the fluorescent analyte suitable for administration to the subject.

100. A computer program product according to Claim 89, further comprising computer program code for confirming micelle concentration at a target site before stimulating toxin release based on the confirmation.

101. A computer program product according to Claim 100, further comprising monitoring for the expression of a protein produced from a gene therapy modification.

102. A computer program product according to Claim 89, wherein the computer program product further comprises computer readable program code for evaluating selected predictive variables or parameters associated with at least one of the uptake and retention of the fluorescent analyte in the localized tissue.

103. A computer program product according to Claim 102, wherein the code evaluates at least one of: the amount of time the detected fluorescence intensity level is above a predetermined threshold level, the amount of time that the detected fluorescence intensity is increasing, the peak value of the detected fluorescence intensity, the time at which the peak fluorescence level occurs, and the decay rate of the detected fluorescence intensity.

104. A computer readable program code according to Claim 89, further comprising computer program code for determining a projected phenotypic response to the fluorescent analyte.